UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/073,260	02/13/2002	Domenica Simms	0942.5170001/RWE/ALS	6799

26111 7590 03/23/2005

STERNE, KESSLER, GOLDSTEIN & FOX PLLC
1100 NEW YORK AVENUE, N.W.
WASHINGTON, DC 20005

EXAMINER	
BAUSCH, SARAE L	

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 03/23/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/073,260	SIMMS ET AL.	
	Examiner	Art Unit	
	Sarae Bausch	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 December 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-32 and 55-63* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-32 and 55-63* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Detailed action*.

DETAILED ACTION

1. Currently, claims 1-31 and 55-63 are pending in the instant application. Claim 32-54 and 64-65 have been canceled. All the amendments and arguments have been thoroughly reviewed but were found insufficient to place the instantly examined claims in condition for allowance. The following rejections are either newly presented, as necessitated by amendment, or are reiterated from the previous office action. Response to arguments follow. This action is FINAL.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Withdrawn Rejections

3. The rejections of claim 1, under 35 U.S.C. 112, second paragraph, made in section 4, page 2 of the previous office action, is withdrawn in view of the arguments made in section I-A, page 9-10 of the response mailed 12/27/2004. The arguments were found persuasive and the rejection has been withdrawn.

4. The rejections of claims 13, 15, 27, 29, and 62, under 35 U.S.C. 112, second paragraph, made in section 4, page 2-3 of the previous office action, is withdrawn in view of the amendment to the claims.

Claim Interpretation

The recitation "wherein the pore size of said filter increases in the direction of sample

flow" in claims 1, 31 and 55 is not defined. The claims have been given their broadest reasonable interpretation to encompass a first filter that has a decreased pore size in relation to the second filter, and that the pore size increases in the direction of sample flow.

The recitation "frit" is not defined in the specification or claims. It has been given the broadest reasonable interpretation to be any porous filter material that retains fine particles.

Maintained Rejection

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 1-18, 21-23, 25, 28-31, 55-59, and 61-63 are rejected under 35 U.S.C. 102(b) as being anticipated by Jones (PCT WO95/02049). Jones teaches a method of separating biological compounds from cells by filtration using two filters with increasing pore size in the direction of sample flow.

With regard to claim 1, Jones (WO95/02049) teaches a method of purifying DNA (biological macromolecule) from *E. coli* bacterial culture (biological sample) by passing the cells through a 1 μm filter followed by a 20μm filter (page 22, 1st full paragraph). Jones et al. teaches that the method can be used for genomic DNA (see page 4, 1st paragraph). Jones et al. teaches two filters that have the inherently property of shearing genomic DNA, as evidenced by applicant's own specification (see page 13, last paragraph to page 14, 1st line).

With regard to claim 2, Jones teaches the method of purifying nucleic acid from cells that comprises lysing a cell suspension to form a cell lysate containing nucleic acid and applying the cell lysate to a filter to remove unwanted cells and cell debris (page 2, 4th full paragraph).

With regard to claims 3-5, Jones teaches that any cell producing a target compound may be used in their invention. Jones defines a "cell" to encompass bacterial cells, cells from higher organisms for example blood cells, phage particles, and other cell types or organelles which contain the target compound and may require some form of lysis step to release it (page 3, 4th full paragraph). The cells are lysed prior to applying to the first filter (page 2, 4th full paragraph).

With regard to claims 6-11, Jones teaches that the target compound to be separated may comprise nucleic acid (instant claim 6), protein, or other desired compounds, in particular purifying recombinant proteins and antibodies (instant claim 7)(page 2, 2nd and 3rd paragraph). Jones further teaches that RNA or DNA may be purified using this invention (page 5, 2nd paragraph) (instant claim 8-11).

With regard to claims 12-18, Jones teaches the use of two filter layers to purify DNA from bacterial cells, with the first filter layer having 1μm pore size (instant claims 12-14) and the second filter layer having 20 μm pore size (instant claims 15-18) (page 22, 1st full paragraph).

With regard to claims 21-23 and 25, Jones teaches the use of a first filter layer that retains unwanted cells and cell debris (instant claim 21), that is made of any material that can tolerate the reagents such as cellulose acetate (acetylated cellulose) (instant claim 25) and is no greater than 50 μm in pore size and no smaller than .2 μm (instant claim 22-23) (page 6, 1st full paragraph).

With regard to claim 28 and 29, Jones teaches the method of a membrane filter that is placed inside the column (tube) (instant claim 29) and has a cylindrical shape (instant claim 28) (page 11, last paragraph, figure 1 and figure 2).

With regard to claims 30-31, Jones teaches the method of lysing a cell suspension to form a cell lysate, applying the cell lysate to a filter to remove unwanted cells and cell debris, contacting the filtered lysate with a solid phase matrix, separating the resultant filtered lysate from the matrix, and eluting the nucleic acid from the matrix (page 2, 4th full paragraph). Jones teaches the method of purifying plasmid DNA by using a filtration method of increasing pore sizes of two filters using a 1 μm filter followed by a 20 μm filter and promoting the flow of lysate through the filters by positive pressure (page 22, 1st full paragraph).

With regard to claim 55-59 and 61-62, Jones teaches the method of lysing a cell suspension from *E. coli* (natural source) to form a cell lysate, applying the cell lysate to a filter to remove unwanted cells and cell debris, followed by contacting the filtered lysate with a solid phase matrix, separating the resultant filtered lysate from the matrix, and eluting the nucleic acid from the matrix (page 2, 4th full paragraph). Jones teaches the method of purifying plasmid DNA (instant claim 57) by the method of increasing the pore sizes of the filters (instant claim 55 and 59), by using a 1 μm cellulose acetate filter followed by a 20 μm PTFE filter (instant claim 61-62) and promoting the flow of lysate through the filters by positive pressure (instant claim 56) (page 22, 1st full paragraph and Table 1, page 21).

With regard to claim 63, Jones teaches an assembly of multiple columns that can process multiple samples simultaneously (figure 3 and page 14, 2nd full paragraph).

Response to Arguments

7. The response traverses, on page 12-14 of the response mailed 12/27/2004, that Jones does not describe shearing genomic DNA and the skilled artisan upon reading Jones' protocol would expect that the first filter retained cell debris and allowed genomic DNA to pass through and therefore Jones' does not teach all the limitation of the Applicants' independent claims as amended. Applicant's arguments have been thoroughly reviewed but are not found persuasive because although Jones does not specifically recite that the genomic DNA is sheared, such is an inherent property of both filters taught by Jones (see page 6, 1st paragraph). As evidenced by applicant's own specification, which teaches "a second population of pores sufficient to shear genomic DNA....pore size may range from about 0.1 μm to about 500μm" (see page 13, last paragraph cont'd to page 14, 1st line). Therefore, Jones' inherently teaches a filter with a pore size that shears genomic DNA (see page 21, table 1, upper filter of 1 μm and lower filter of 20 μm). Applicant's further assert that the skilled artisan upon reading Jones' protocol would expect that the first filter retained cell debris and allowed genomic DNA to pass through, however crude DNA could contain sheared genomic DNA. Additionally, Jones teaches a second filter of 20 μm that elutes DNA, however a filter size of 20 μm would inherently shear genomic DNA, as evidenced by applicants own specification (see above), therefore a skilled artisan upon reading Jones' protocol would expect the filters to shear genomic DNA. For these reasons, and the reasons made of record in the previous office actions, the rejection is maintained.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 19 and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jones (WO95/02049) in view of Dewitt (US Patent 6183645)

Jones (WO95/02049) teaches the method of lysing a cell suspension to form a cell lysate, applying the cell lysate to a filter to remove unwanted cells and cell debris, followed by contacting the filtered lysate with a solid phase matrix, separating the resultant filtered lysate from the matrix, and eluting the nucleic acid from the matrix (page 2, 4th full paragraph). Jones teaches the method of purifying DNA by increasing the pore sizes of two filters or two filter layers, having a first cellulose acetate filter layer followed by a second PTFE filter, which can be considered a "frit" (page 22, 1st full paragraph and Table 1, page 21). Jones et al. teaches that the method can be used for genomic DNA (see page 4, 1st paragraph). Jones et al. teaches two filters that have the inherently property of shearing genomic DNA, as evidenced by applicant's own specification (see page 13, last paragraph to page 14, 1st line). Jones does not teach the use

of the second filter layer which is polypropylene (claim 24) and is composed of two frits (claim 19).

DeWitt ('645) teaches the method of phase separation using one or more polypropylene frits (column 3, lines 46-50) and teaches the use of the improved apparatus for purification and isolation (column 1, lines 50-64).

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to improve in the method of Jones to substitute in the second filter layer of Jones, two polypropylene frits as taught by Dewitt, to improve the method of Jones by providing a system that is more amenable to automation, facilitates more efficient and faster simultaneous purification and isolation, and is less expensive and easier to manufacture as taught by DeWitt (column 1, lines 55-64). The ordinary artisan would have been motivated to improve the method of Jones with the use of two frits in the second filter layer as taught by DeWitt, for the purpose of improving the method of Jones so as to include a second frit within the second filter layer to insure better separation or isolation of the biological macromolecule. The ordinary artisan would have had a reasonable expectation of success that using a second frit in the method of Jones would yield improved and faster separation because DeWitt teaches that the use of two or more frits insures better results and faster purification, separation, and isolation techniques.

11. Claim 20 is rejected under 35 U.S.C. 103(a) as being unpatentable over Jones (WO95/02049) as applied to claim 19 and 24 above, and further in view of Fung et al (US Patent 6221655).

The method of Jones in view of Dewitt (US Patent 6183645) is set forth in section 9 above. Jones in view of DeWitt does not teach the thickness of the two filter frits in the second filter layer.

Fung et al ('655) teaches the use of a filter frit made of porous low protein binding material such as polyethylene or polypropylene (see column 4, lines 64-66) with a thickness of .03-.04 in. (.16 mm) (see column 5, lines 11-19) in a spin filter assembly to facilitate the isolation of compounds, such as proteins, present in various biological samples (see column 6, lines 64-66). Furthermore, Fung et al. teaches the addition of a solid binding matrix to the spin frit filter assembly unit (see column 6, lines 65- 67 and column 7, lines 1-5). The thickness of "about" 1/16 of an inch is broadly interpreted to encompass 0.03-0.04 inches (0.16 mm).

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to use a filter frit of about 0.16 mm thickness as disclosed by Fung et al. in the second filter layer (two frits) of Jones in view of DeWitt. While Jones in view of DeWitt does not disclose the thickness of each frit, Fung et al. teaches that the thickness of a polyethylene frit is, for example, 0.03-0.04 in (0.16 mm). The ordinary artisan would have been motivated to include a frit with a thickness of 0.16 mm, as Fung et al. teaches that polyethylene or polypropylene frits used in isolation of biological macromolecules is about 0.03-0.04 inches. The instant claimed recitation of a frit of about 1/16 of an inch is obvious over the disclosure of Jones in view of DeWitt and further in view of Fung et al, absent secondary considerations.

12. Claims 26 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jones (WO95/02049) in view of Sirkar (US Patent 5053132)

Jones (WO95/02049) teaches the method of lysing a cell suspension to form a cell lysate, applying the cell lysate to a filter to remove unwanted cells and cell debris, followed by contacting the filtered lysate with a solid phase matrix, separating the resultant filtered lysate from the matrix, and eluting the nucleic acid from the matrix (page 2, 4th full paragraph). Jones teaches the method of purifying DNA by said method using increasing pore sizes of two filters, having a first cellulose acetate filter with a pore size of .2 μm followed by a second PTFE filter with a pore size of 20 μm (page 22, 1st full paragraph and Table 1, page 21). Jones et al. teaches that the method can be used for genomic DNA (see page 4, 1st paragraph). Jones et al. teaches two filters that have the inherently property of shearing genomic DNA, as evidenced by applicant's own specification (see page 13, last paragraph to page 14, 1st line). Jones does not teach the use of regenerated cellulose.

Sirkar ('132) teaches the use of a regenerated cellulose and polyethylene composite filter (see column 3, lines 62-68 and column 4, lines 1-9). Sirkar teaches the use of regenerated cellulose for use as a membrane for its enhanced solvent resistance properties over cellulose acetate membrane (column 4, lines 26-27) and the ability of the regenerated cellulose membrane to bind cellular debris and other biological materials (column 8, lines 3-13).

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to improve the method of Jones, by modifying the first filter containing cellulose acetate of Jones to include a regenerated cellulose membrane as taught by Sirkar, and the second filter composed of PTFE of Jones to include a support layer of polyethylene as taught by Sirkar, to improve the method of Jones to allow for better separation using a membrane that binds cellular debris, as taught by Sirkar. The ordinary artisan would

have been motivated to improve the first filter layer of cellulose acetate in the filter assembly of Jones to include a regenerated cellulose membrane and the second filter layer of PTFE to a polyethylene membrane method taught by Sirkar for the purpose of improving the separation of the cell lysate to include a membrane that binds cellular debris and other unwanted biological compounds. The ordinary artisan would have had a reasonable expectation of success that using a porous hydrophilic regenerated cellulose membrane with a porous layer of polyethylene could be used to modify the filter assembly method of Jones because Sirkar teaches the use of regenerated cellulose membrane with a porous support of polyethylene prevent cellular debris from contaminating the final sample by immobilizing the cellular debris on a porous hydrophilic side of the membrane (column 8, lines 3-7).

13. Claims 24 and 60 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jones in view of Fung et al (US Patent 6221655).

Jones teaches the method of lysing a cell suspension to form a cell lysate, applying the cell lysate to a filter to remove unwanted cells and cell debris, followed by contacting the filtered lysate with a solid phase matrix, separating the resultant filtered lysate from the matrix, and eluting the nucleic acid from the matrix (page 2, 4th full paragraph). Jones teaches the method of purifying DNA by said method using increasing pore sizes of two filters, having a cellulose acetate filter with the pore size of 1 μm followed by a PTFE filter with the pore size of 20μm (page 22, 1st full paragraph and Table 1, page 21). Jones et al. teaches that the method can be used for genomic DNA (see page 4, 1st paragraph). Jones et al. teaches two filters that have the inherently property of shearing genomic DNA, as evidenced by applicant's own specification (see page 13, last paragraph to page 14, 1st line). Jones does not teach the thickness of the filter

bed (claim 60), nor the use of a polyethylene frit for a second filter or filter layer (claim 24). The term "filter bed" is not defined by the specification. The term has therefore been given its broadest reasonable interpretation to encompass either the lower filter of a multiple filter assembly, or the entire thickness of a filter assembly comprising more than one filter, wherein the filters are stacked, in contact, each on top of the next.

Fung et al ('655) teaches the use of a filter frit as a second filter layer made of porous low protein binding material such as polyethylene or polypropylene with a thickness of .03-.04 inches (0.16 mm) (column 5, lines 11-19) in a spin filter assembly (binding matrix can be added as a first layer) to facilitate the isolation and analysis of biological macromolecules present in various biological samples (column 6, lines 64-66).

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to use a filter bed of about 0.16 mm thickness as disclosed by Fung et al. in the second filter layer of Jones. While Jones does not disclose the thickness of the filter bed, Fung et al. teach that the thickness of a polyethylene frit is for example, .03-.04 inches (0.16 mm). The ordinary artisan would have been motivated to include a filter bed thickness of 0.16 mm, as Fung et al. teach that polyethylene or polypropylene frits used in isolation of biological macromolecules is about .03-.04 inches (0.16 mm). The instant claimed recitation of a filter bed of thickness being from 0.1 mm to 10 mm is obvious over the disclosure of Jones in view of Fung et al., absent secondary considerations.

Response to Arguments

14. The response traverses, on page 14-17 of the response mailed 12/27/2004, that neither DeWitt, Sirkar, Fung, or Jones teach a filter that shears genomic DNA and therefore the

references do not teach or suggest all the claim limitations. Applicant's arguments have been thoroughly reviewed but are not found persuasive because as set forth in section 7 above, although Jones does not specifically recite that the genomic DNA is sheared, such is an inherent property of both filters taught by Jones (see page 6, 1st paragraph). As evidenced by applicant's own specification, which teaches "a second population of pores sufficient to shear genomic DNA....pore size may range from about 0.1 μm to about 500μm" (see page 13, last paragraph cont'd to page 14, 1st line). Therefore, Jones' inherently teaches a filter with a pore size that shears genomic DNA (see page 21, table 1, upper filter of 1 μm and lower filter of 20 μm). For these reasons, and the reasons made of record in the previous office actions, the rejection is maintained.

Conclusion

15. No claims are allowable.

16. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sarae Bausch whose telephone number is (571) 272-2912. The examiner can normally be reached on M-F 10am-7pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones can be reached on (571)272-0745. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Jehanne Sitton

JEHANNE SITTON
PRIMARY EXAMINER

3/18/05

Sarae Bausch
Examiner
Art Unit 1634